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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
09/335,686	06/18/99	NOELLE	R 012712-696

EXAMINER

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 11/14/00

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1998-421-632/40206

DETAILED ACTION

1. Applicant's election of Group I and the species anti-gp39 antibodies in Paper No. 5 without traverse is acknowledged.

However, upon a review of the instant application, it is noted claims 2-43 were canceled in applicant's preliminary amendment, filed 6/18/99.

Claim 1 is the sole pending claim in the instant application.

2. Applicant should amend the first line of the specification to cross reference related applications and update the status of priority documents.
For example, USSN 08/475,873 is now U.S. Patent No. 5,942,229.
And the proper designation of the earliest priority document is USSN 08/115,990 (not 08/111,990).
Also, applicant should indicate priority to PCT/US94/09872 indicated in the oath/declaration.

3. Formal drawings have been submitted which comply with 37 CAR 1.84.

4. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to methods of inhibiting a humoral immune response to a TD antigen in vivo by administering the TD antigen "with an antagonist of a molecule on a Th cell which mediates contact-dependent helper effector function"

Such "antagonists" with specificity for "a molecule on a Th cell which mediates contact-dependent helper effector function" do not meet the written description provision of 35 USC 112, first paragraph. There is insufficient guidance and direction as to the written description of these "antagonists" and "Th cell molecules" intended and encompassed by the claimed agents and compositions.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed "antagonists" and "Th molecules" and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or screening for said "antagonists" or "Th molecules".

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483.

In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.
Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Therefore, there is insufficient written description for the "antagonists" and "Th molecules" under the written description provision of 35 USC 112, first paragraph.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "antibodies that bind gp39" or "soluble CD40/CD40-Ig"; does not reasonably provide enablement for any "antagonist of a molecule on a Th cell which mediates contact-dependent helper effector function".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunosuppressive drugs such as immunologically-based biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the experimental observations of inhibiting certain immune responses with "antibodies that bind gp39" or "soluble CD40/CD40-Ig" enables any "antagonist of a molecule on a Th cell which mediates contact-dependent helper effector function".

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Applicant has not provided any biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies or enables any "antagonist of a molecule on a Th cell which mediates contact-dependent helper effector function" other than "antibodies that bind gp39" or "soluble CD40/CD40-Ig".

It is not sufficient to define a specificity by an ill-defined functional property or ambiguous structural properties (e.g. "antagonist of a molecule on a Th cell which mediates contact-dependent helper effector function"). See Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992). Also, an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property (e.g. structural or functional of inhibiting Th helper function)). Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed interrupter agents in a manner reasonably correlated with the scope of the claims broadly including any number of possible "antagonists of a molecule on a Th cell which mediates contact-dependent helper effector function".

For example, since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

Minor structural differences among structurally related compounds or compositions can result in substantially different pharmacological activities. Therefore, structurally unrelated compounds encompassed by the claimed "antagonists of a molecule on a Th cell which mediates contact-dependent helper effector function" would be expected to have greater differences in their activities.

However, applicant has not provided limited biochemical information for the particular claimed "antagonists of a molecule on a Th cell which mediates contact-dependent helper effector function". Therefore, the problem of predicting protein structure from such information from a limited number of antagonists as they pertain a particular Th antigen (e.g. gp39, CD40L or CD40 ligand) and, in turn, utilizing predicted structural determinations to ascertain functional aspects of an appropriate "antagonist of a molecule on a Th cell which mediates contact-dependent helper effector function" and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Insufficient direction or guidance is provided to assist one skilled in the art in the selection of any other "antagonist of a molecule on a Th cell which mediates contact-dependent helper effector function" nor is there sufficient evidence provided that other certain "antagonists" for any "Th molecule" can inhibit humoral immune responses , commensurate in scope with the claimed methods.

The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, making and using the claimed "antagonists of a molecule on a Th cell which mediates contact-dependent helper effector function" would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Applicant should consider amending the claims to limit the invention to targeting gp39 or CD40 ligand on T helper cells with gp39-specific antibodies or soluble CD40.

8. Claim 1 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation of "TD" and "Th" and "TI-2" because these terms should be spelled out to clearly define their meaning, at least upon first time usage.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

10. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of.35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 1 is rejected under 35 U.S.C. § 102(e) as being anticipated by Cobbold et al. (U.S. Patent No. 6,056,956) . Cobbold et al. teach the use of CD4-specific antibodies to induce specific non-responsiveness or tolerance to various molecules, including globular proteins, glycoproteins and polypeptides intended for therapeutic use (see entire document, including column 2, lines 58-67) Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods, given that CD4 is expressed on T helper cells.

12. Claim 1 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Cobbold et al. (U.S. Patent No. 6,056,956) in view of Lederman et al. (U.S. Patent No. 5,474,771; 1449, #AA) OR Armitage et al. (U.S. Patent No. 6,087,329).

Cobbold et al. teach the use of CD4-specific antibodies to induce specific non-responsiveness or tolerance to various molecules, including globular proteins, glycoproteins and polypeptides intended for therapeutic use (see entire document, including column 2, lines 58-67)

Cobbold et al. Differs from the claimed methods by not teaching the preferred embodiments of targeting the CD40L/gp39 with CD40L-specific antibodies.

Lederman et al. teach inhibiting various immune responses with 5C8-specific antibodies (see entire document, including columns 6-7, 11). The 5C8 specificity is the equivalent of human CD40L.

Armitage et al. teach inhibiting various immune responses with CD40 antagonists, including soluble CD40, CD40lg, monomeric CD40L (e.g. columns 10-11, including overlapping paragraph, columns 14-17; column 21)

Given the ability of 5C8-/CD40l-specific antibodies, as taught by Lederman et al. OR the ability of various CD40 antagonists, as taught by Armitage et al. to inhibit various immune responses, including T helper cell-mediated immune responses, including humoral responses; one of ordinary skill in the art at the time the invention was made would have been motivated to substitute these antagonists into the methods of Cobbold et al. To similarly target T helper cells to inhibit humoral responses to thymus-dependent antigens. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 5,942,229.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims anticipate the instant method claims.

In addition, when the instant claims are read in light of the specification; the patented claims are the preferred embodiments and again anticipate the instant claims.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, Ph.D.
Primary Examiner
Technology Center 1600
January 29, 2001